Emergency arising from patients' fear of taking antimalarials during these COVID-19 times: are antimalarials as unsafe for cardiovascular health as recent reports suggest?

We read with interest the paper of Graef *et al* recently published in your journal about the situation resulting from the massive use of antimalarials for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2/COVID-19), despite the fact that the evidence is controversial and there are concerns about its possible cardiotoxicity, leaving rheumatic patients who use them in a position of vulnerability due to medication shortages.[1] In the past few weeks, several papers have been published about the efficacy and safety of the antimalarials chloroquine (CLQ) and hydroxychloroquine (HCLQ) for the treatment of the different phases of infection by SARS-CoV-2/COVID-19, and the data are controversial. However, it is striking that some studies report high rates of cardiovascular events (CVEs) associated mainly with cardiac arrhythmias.[2] .

These findings of adverse CVEs reported in the aforementioned studies have unfortunately led to the emergency in this group of patients around fear of chronic use of antimalarials, and many users are abandoning these medications, which implies great clinical risk due to relapses that may appear.[3] On the other hand, the massive use of antimalarials for COVID-19 has resulted in medication shortages in some settings with potential consequences to patients users.

Antimalarials have been used for several decades for the treatment of malaria and some autoimmune diseases, mainly rheumatoid arthritis (RA) and lupus, with great utility and efficacy, and also great safety at conventional doses (250 mg per day of CLQ and 200–400 mg per day of HCLQ).[4]

We show a real-life experience in a rheumatic centre in Bogota, Colombia. We performed a retrospective cohort analysis of adverse events (AEs), adverse reactions (ARs) and medication-related problems (MRPs) presented in the last 16 months, according to the methodology of the Third Consensus of Granada. The severity of the events and reactions was evaluated using the Dader Method of therapeutic drug monitoring, and the Naranjo algorithm was used to characterise them as AEs, ARs or MRPs.

Here, we report the outcomes since 1 January 2019–30 April 2020. By the end of 2018, there were 1004 patients with RA using antimalarials; currently, there are 660 patients still using CLQ/HCLQ; 583 (88.3%) are using CLQ and 77 (11.7%) are using HCLQ; of them, 186 (28.2%) patients have cardiovascular comorbidities, previous to antimalarial use, like primary hypertension, cardiovascular disease or the two combined (table 1).

Regarding safety concerns during observation period, 344 patients presented with AEs and ARs that required the withdrawal of antimalarials; of them, 130 (37.9%) had retinal toxicity an expected AR; 103 (30%) had gastrointestinal intolerance, accepted as an AE; 110 (31.8%) had different types of dermatological ARs; 1 patient had severe dizziness, possibly an MRP; and there were no CVEs or arrhythmias, despite the fact that 95 (27.6%) patients previously had cardiovascular comorbidity (table 2).

Table 2 Adverse events and reactions to antimalarials in patients with rheumatoid arthritis during observation period

AE/AR	Patients without CVD/PH (n=249)	Patients with previous CVD/PH (n=95)	Total n=344 (%)
Retinal toxicity	100	30	130 (37.9)
Gastrointestinal AEs	83	20	103 (30.0)
Dermatological ARs	65	45	110 (31.8)
Severe dizziness	1	0	1 (0.3)
CVD AEs/ARs	0	0	0 (0.0)

AE, adverse event; AR, adverse reaction; CVD, cardiovascular disease; PH, primary hypertension.

At first glance, these results seem surprising; there are zero incidences of new, incidental CVE in this RA cohort using antimalarials, although of course, we are talking about different doses for RA and COVID-19; on the contrary, CLQ and HCLQ have been associated with a reduced risk of CVE in patients with rheumatic diseases through robust research,[5] in addition to the finding that the use of HCLQ is independently associated with decreased risk for cardiovascular morbidity among patients with RA.[6] AEs and ARs presented by these patients are consistent with data previously published but reinforce the fact that antimalarials are drugs that lack cardiotoxicity in rheumatic patients; therefore, education for doctors and patients in general must be reinforced to prevent antimalarials from being abandoned because of the past news.

Pedro Santos-Moreno ,[1] **Diana Buitrago-Garcia,**[2] **Laura Villarreal,**[1] **Anggie Aza,**[1] **Michael Cabrera,**[3] **Wilberto Rivero,**[4] **Adriana Rojas-Villarraga**[5]

[1]Rheumatology, Biomab IPS, Bogotá, Colombia
[2]Epidemiology, Biomab IPS, Bogotá, Colombia
[3]Statistics and Clinical Reports, Biomab IPS, Bogotá, Colombia
[4]Pharmacy and Pharmacovigilance, Biomab IPS, Bogotá, Colombia
[5]Research Department, Fundación Universitaria de Ciencias de la Salud-FUCS, Bogotá, Colombia

Correspondence to Dr Pedro Santos-Moreno, Rheumatology, Biomab IPS, Bogotá, Colombia; pedrosantosmoreno@hotmail.com

Acknowledgements We acknowledge the support staff, administrative staff and all the members of the healthcare work group developing the Rheumatoid Arthritis T2T programprogramme in Biomab IPS.

Table 1 Cardiovascular disease in patients with rheumatoid arthritis currently and previously using antimalarials

	Currently users of antimalarials			Previous users of antimalarials withdrawn by adverse events		
Comorbidities	CLQ (n=583)	HCLQ (n=77)	Total n=660 (%)	CLQ (n=330)	HCLQ (n=14)	Total n=344 (%)
PH	140	16	156 (23.5)	74	1	75 (21.8)
CVD	10	4	14 (2.1)	3	0	3 (0.9)
PH and CVD	15	1	16 (2.4)	16	1	17 (4.9)
No CVD/PH comorbidities	418	56	474 (72.0)	237	12	249 (72.4)

CLQ, chloroquine; CVD, cardiovascular disease; HCLQ, hydroxychloroquine;PH, primary hypertension.